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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/987,107	11/13/2001	Jonas Graversen	GRAVERSEN=1A	6444

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BROWDY AND NEIMARK, P.L.L.C.
624 NINTH STREET, NW
SUITE 300
WASHINGTON, DC 20001-5303

EXAMINER	
SNEDDEN, SHERIDAN	

ART UNIT	PAPER NUMBER
1653	

DATE MAILED: 02/11/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/987,107	GRAVERSEN ET AL.	
	Examiner	Art Unit	
	Sheridan K Snedden	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the corresp ndence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/21/2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-84* is/are pending in the application.

4a) Of the above claim(s) *63-84* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-64* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____.
4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment of claims 5 and 42 in paper filed 29 January 2002 is acknowledged. Applicant's amendment of claims 2, 10, 14, 32, 33, 36, 37, 43, 50, 53, 58, 62, 64, 68, 70, 71, 72, 73, 81, and 82 filed 9 July 2002 is acknowledged

2. Applicant's election of invention I, claims 1-62 is acknowledged. Claims 63-84 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **with** traverse in Paper filed 21 October 2003.

3. The traversal is on the ground(s) that the claims are allowable or that the search would not be burdensome. This is not found persuasive because there is no allowable generic or linking claim (see below). Additionally, the invention of Groups I-IV are directed to patentably distinct subject matter that have acquired a separate status in the art because of their recognized divergent subject matter. As such, a different search is required. The requirement is still deemed proper and is therefore made FINAL.

Claim Rejections - 35 USC § 112

4. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one

skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is also referred to the Guidelines on Written Description published at FR 66(4) 1099-1111 (January 5, 2001) (also available at www.uspto.gov). The following passage is particularly relevant.

> The written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. A "representative number of species" means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within a genus, one must describe a sufficient number of species to reflect the variation within the genus. What constitutes a "representative number" is an inverse function of the skill and knowledge in the art. Satisfactory disclosure of a "representative number" depends on whether one of skill in the art would recognize that applicant was in possession of the necessary common attributes or features of the elements possessed by the members of the genus in view of the species disclosed. In an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus.

Claims 1-62 are directed to fusion proteins comprising Apo-A, and all variants and functional analogs of Apo-A. The specification discloses specific homologs and isoforms of Apo-A. However, the specification does not provide all naturally occurring variants, mutants, functional ananlogs, or guidance regarding how to obtain specific mutants, variants or functional analogs at that retain the function of the Apo-A protein.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

With the exception of Apo-AI, Apo-AII, Apo-AIV or Apo-E, the skilled artisan would not have envisioned the detailed chemical structure of the encompassed polypeptides and functional analogs, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, only Apo-AI, Apo-AII, Apo-AIV or Apo-E, but not the full breadth of the claim, meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

5. Claims 27-29, 35-36, 57-59, 62 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 27-29, 35-36, 57-59, 62 are directed in part to a polypeptide comprising at least 68% sequence similarity with a Trip A

module or a polypeptide comprising at least 70% sequence similarity to SEQ ID NO: 2, 3, 11, 14. The specification discloses concepts regarding the meaning of "percent" (%) (page 32-33); however, there is no description of the differences brought about by a percent similarity difference (e.g., if there is a similarity difference of 73, 86 or 92%) that would result in a biologically active protein. That is, what is the specific biological function that is retained by the percent identity. Applicants may wish to amend the claim to delete the 68% or 70% identity language, and indicate a specific, measurable function.

6. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 15-30, 38 and 58 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The term "construct" in claims 1 and 38 are used by the claim to mean "a protein construct", while the term generally connotes "a nucleic acid construct." The term is indefinite because the specification does not clearly redefine the term and, when read in isolation of the remaining claims, the claims do not distinguish between nucleic acids and protein.

The term "substantially" in claim 4 is a relative term which renders the claim indefinite. The term " substantially " is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

Claims 15-30 recite the limitation for "the oligomerising module." There is insufficient antecedent basis for this limitation in the claims.

Claims 28 and 58 are indefinite because they contain a multiplicity of periods "." (see "no."). Absent factual evidence to the contrary the claim ends at the first period. Claims are defined by being single sentence format.

Claim Rejections - 35 USC § 102

7. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

8. Claims 1-4, 7, 8, 11-14, 32, 33, 35-41, 43-49 and 62 are rejected under 35 U.S.C. 102(b) as being anticipated by Smith *et al.* (US 5,408,038). Smith *et al.* teach a fusion protein comprising human Apo-B and human Apo AI (see column 6, line 20 for example; regarding claims 1, 7, 8, 11, 14, 43, 44). The last element of claim 1 recites a conditional element that does not apply to the instant reference. The apo-B taught by Smith *et al.* is an oligomerizing protein that would be terminally linked to Apo-A (regarding claim 38, 46). The vector construct taught by Smith *et al.* contains a linker sequence that would translate into two or more amino acids (column 6, line 60; regarding claims 2-4, 39-41). Apo B would read upon the limitation of a variant eliciting substantially the same physiological response to Apo AI (regarding claims 12, 13, 44, 45). The binding of proteins such as CETP is an inherent property of Apo-A (see Bruce *et al.*; regarding claim 33). The composition of Smith *et al.* is taught as a composition that is pharmaceutically acceptable (regarding claim 37). The ability of apolipoproteins to oligomerize

is an inherent proprerty of the molecules, including dimerizsing, trimerising and tetramerising (see Osborne *et al.*, for example; regarding claims 46-49). human Apo-B and human Apo AI both share greater than 70% identity with SEQ ID NO: 2, 3, 11, and 14 (claims 35, 36, 62). Thus, the reference anticipates the claimed invention.

9. Claims 1-4, 6- 8, 10-14, 15, 18, 32, 33, and 35-37 are rejected under 35 U.S.C. 102(b) as being anticipated by Sirtori *et al.* (US 5,876,968). Sirtori *et al.* teach apolioprotein A1-M fused to a modified IgG (see column 4, lines 5-25; regarding claims 1, 6-8, 10-14, 32, 33, 37). A1-M would share greater than 70% indentity with SEQ ID NO: 2, 3, 11, and 14 (claims 35, 36). The major structural requirement of the Apo Al molecule is believed to be the presence of repeat units of 11 or 22 amino acids, presumed to exist in amphipathic helical conformation (claim 11). Apo Al-M has the capacity to form dimers with itself and complexes with Apo All (claims 15, 18). The fusion protein contains a substantially linear spacer sequence that is cleavable with formic acid (regarding claims 2-4). Thus, the reference anticipates the claimed invention.

Conclusion

10. No claims are allowed. The prior art does not teach the use of tetranectin in combination with Apo-A fusion proteins.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sheridan K Snedden whose telephone number is (571) 272-0959. The examiner can normally be reached on Monday - Friday, 8:30 AM to 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone number for regular communications to the organization where this application or proceeding is assigned is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

SKS
February 9, 2004

SKS

CHRISTOPHER S. F. LOW
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600